

Amendments to the Claims:

Please amend claims 7 and 25-30, and add new claims 31-73. Claims 1-6 and 8-24 are canceled. This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1-6. (Canceled)

7. (Currently Amended): [[An]] A nucleic acid composition comprising: a nucleic acid vector having at least one cytosine to non-cytosine substitution within a CpG motif, wherein the CpG motif is of the formula 5' purine-pyrimidine C-G-pyrimidine-pyrimidine-3' or 5' purine-purine C-G-pyrimidine-pyrimidine-3', and wherein the cytosine to non-cytosine substitution is within the CpG dinucleotide comprising a nucleic acid sequence of SEQ ID NO:297, wherein nucleotides at positions 784, 1161, 1218, 1264, 1337, 1829, 1831, 1874, 1876, 1940, 1942, 1963, 1966, 1987, 1997 and 1999 are as follows:

G at nucleotides 784, 1161, 1218, 1831, 1876, 1942, 1966 and 1999;

A at nucleotides 1264, 1337, 1829, 1874, 1940 and 1997; and

T at nucleotides 1963 and 1987.

8-24. (Canceled)

25. (Currently Amended): The nucleic acid composition of claim 7, wherein the ~~nucleic acid vector~~ composition further comprises an immune ~~modulatory~~ inhibitory nucleic acid sequence (IIS) comprising a hexamer region of the formula 5'-Purine-Purine-[X]-[Y]-Pyrimidine-Pyrimidine-3'; wherein X and Y are any naturally occurring or synthetic nucleotides except that X and Y cannot be cytosine-guanine.

26. (Currently Amended): The ~~method~~ nucleic acid composition of claim 25, wherein the ~~immune-modulatory-nucleic-acid~~ IIS further comprises a polyG region linked 5' or 3' to the hexamer region.

27. (Currently Amended): The ~~method~~ nucleic acid composition of claim 25, wherein the ~~immune-modulatory-nucleic-acid~~ IIS further comprises a first polyG region linked 5' to the hexamer region and a second polyG region linked 3' to the hexamer region.

28. (Currently Amended): The nucleic acid composition of claim 7, wherein the ~~nucleic-acid-vector~~ composition further comprises an ~~immune-modulatory-nucleic-acid~~ IIS comprising a hexamer region of the formula 5'-Purine-Pyrimidine-[X]-[Y]-Pyrimidine-Pyrimidine-3', wherein X and Y are any naturally occurring or synthetic nucleotides except that X and Y cannot be cytosine-guanine.

29. (Currently Amended): The ~~method~~ nucleic acid composition of claim 28, wherein the ~~immune-modulatory-nucleic-acid~~ IIS further comprises a polyG region linked 5' or 3' to the hexamer region.

30. (Currently Amended): The ~~method~~ nucleic acid composition of claim 28, wherein the ~~immune-modulatory-nucleic-acid~~ IIS further comprises a first polyG region linked 5' to the hexamer region and a second polyG region linked 3' to the hexamer region.

31. (New): The nucleic acid composition of claim 25, wherein the nucleic acid vector further comprises the IIS.

32. (New): The nucleic acid composition of claim 7, wherein the vector further comprises a polynucleotide encoding an autoantigen targeted in an autoimmune disease.

33. (New): The nucleic acid composition of claim 32, wherein the autoantigen comprises a polynucleotide encoding a myelin protein.

34. (New): The nucleic acid composition of claim 33, wherein the myelin protein is myelin basic protein (MBP).

35. (New): The nucleic acid composition of claim 32, wherein the autoantigen comprises a polynucleotide encoding an insulin protein.

36. (New): The nucleic acid composition of claim 35, wherein the insulin protein is selected from the group consisting of insulin, proinsulin and preproinsulin.

37. (New): The nucleic acid composition of claim 7, further comprising a pharmaceutically acceptable carrier.

38. (New): A composition comprising a modified nucleic acid vector with reduced immunostimulatory properties, the nucleic acid vector modified by a method comprising the steps of:

a) providing an unmodified nucleic acid vector comprising a CpG dinucleotide, wherein the CpG dinucleotide is in a motif of a formula 5'-purine-pyrimidine-C-G-pyrimidine-pyrimidine-3';

b) substituting the cytosine in the CpG dinucleotide to a non-cytosine in the motif in the unmodified vector; thereby producing a modified nucleic acid vector, wherein the modified nucleic acid vector induces a reduced degree of immunostimulation in comparison to the unmodified nucleic acid vector.

39. (New): The composition of claim 38, wherein the cytosine to non-cytosine substitution is cytosine to guanine.

40. (New): The composition of claim 38, wherein a plurality of cytosine to non-cytosine substitutions are made.

41. (New): The composition of claim 40, wherein the plurality of cytosine to non-cytosine substitutions are made outside of a control region of the modified vector.

42. (New): The composition of claim 38, wherein the modified vector is a plasmid or cosmid vector.

43. (New): The composition of claim 38, wherein the composition further comprises an IIS comprising a hexamer region of a formula selected from the group consisting of 5'-Purine-Purine-[X]-[Y]-Pyrimidine-Pyrimidine-3' and 5'-Purine-Pyrimidine-[X]-[Y]-Pyrimidine-Pyrimidine-3'; wherein X and Y are any naturally occurring or synthetic nucleotides except that X and Y cannot be cytosine-guanine.

44. (New): The composition of claim 43, wherein the nucleic acid vector further comprises the IIS.

45. (New): The composition of claim 43, wherein the IIS further comprises a polyG region linked 5' or 3' to the hexamer region.

46. (New): The composition of claim 43, wherein the IIS further comprises a first polyG region linked 5' to the hexamer region and a second polyG region linked 3' to the hexamer region.

47. (New): The composition of claim 38, wherein the unmodified vector is SEQ ID NO:297.

48. (New): The composition of claim 47, wherein the unmodified vector that is SEQ ID NO:297 is modified to comprise the following cytosine to non-cytosine substitutions:

C to G at nucleotides 784, 1161, 1218 and 1966;

C to A at nucleotides 1264, 1337, 1829, 1874, 1940, and 1997; and

C to T at nucleotides 1963 and 1987.

49. (New): The composition of claim 48, wherein the unmodified vector that is SEQ ID NO:297 is further modified to comprise the following cytosine to non-cytosine substitutions: C to G at nucleotides 1831, 1876, 1942, and 1999.

50. (New): The composition of claim 38, further comprising a pharmaceutically acceptable carrier.

51. (New): The composition of claim 38, wherein the modified vector further comprises a polynucleotide encoding an autoantigen targeted in an autoimmune disease.

52. (New): The composition of claim 51, further comprising a polynucleotide encoding a myelin protein.

53. (New): The composition of claim 52, wherein the myelin protein is myelin basic protein (MBP).

54. (New): The composition of claim 51, further comprising a polynucleotide encoding an insulin protein.

55. (New): The composition of claim 54, wherein the insulin protein is selected from the group consisting of insulin, proinsulin and preproinsulin.

56. (New): A method of producing a modified nucleic acid vector with reduced immunostimulatory properties, the method comprising the steps of:

a) providing an unmodified nucleic acid vector comprising a CpG dinucleotide, wherein the CpG dinucleotide is in a motif of a formula 5'-purine-pyrimidine-C-G-pyrimidine-pyrimidine-3';

b) substituting the cytosine in the CpG dinucleotide to a non-cytosine in the motif in the unmodified vector; thereby producing a modified nucleic acid vector, wherein the modified nucleic acid vector induces a reduced degree of immunostimulation in comparison to the unmodified nucleic acid vector.

57. (New): The method of claim 56, wherein the cytosine to non-cytosine substitution is cytosine to guanine.

58. (New): The method of claim 56, wherein a plurality of cytosine to non-cytosine substitutions are made.

59. (New): The method of claim 58, wherein the plurality of cytosine to non-cytosine substitutions are made outside of a control region of the modified vector.

60. (New): The method of claim 56, wherein the modified vector is a plasmid or cosmid vector.

61. (New): The method of claim 56, wherein the composition further comprises an IIS comprising a hexamer region of a formula selected from the group consisting of 5'-Purine-Purine-[X]-[Y]-Pyrimidine-Pyrimidine-3' and 5'-Purine-Pyrimidine-[X]-[Y]-Pyrimidine-Pyrimidine-3'; wherein X and Y are any naturally occurring or synthetic nucleotides except that X and Y cannot be cytosine-guanine.

62. (New): The composition of claim 61, wherein the nucleic acid vector further comprises the IIS.

63. (New): The method of claim 61, wherein the IIS further comprises a polyG region linked 5' or 3' to the hexamer region.

64. (New): The method of claim 61, wherein the IIS further comprises a first polyG region linked 5' to the hexamer region and a second polyG region linked 3' to the hexamer region.

65. (New): The method of claim 56, wherein the unmodified vector is SEQ ID NO:297.

66. (New): The method of claim 65, wherein the unmodified vector that is SEQ ID NO:297 is modified to comprise the following cytosine to non-cytosine substitutions:

C to G at nucleotides 784, 1161, 1218 and 1966;

C to A at nucleotides 1264, 1337, 1829, 1874, 1940, and 1997; and

C to T at nucleotides 1963 and 1987.

67. (New): The method of claim 66, wherein the unmodified vector that is SEQ ID NO:297 is further modified to comprise the following cytosine to non-cytosine substitutions: C to G at nucleotides 1831, 1876, 1942, and 1999.

68. (New): The method of claim 56, further comprising a pharmaceutically acceptable carrier.

69. (New): The method of claim 56, wherein the modified vector further comprises a polynucleotide encoding an autoantigen targeted in an autoimmune disease.

70. (New): The method of claim 69, further comprising a polynucleotide encoding a myelin protein.

71. (New): The method of claim 70, wherein the myelin protein is myelin basic protein (MBP).

72. (New): The method of claim 69, further comprising a polynucleotide encoding an insulin protein.

73. (New): The method of claim 72, wherein the insulin protein is selected from the group consisting of insulin, proinsulin and preproinsulin.